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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/684,268	10/10/2003	Felix A. Montero-Julian	2512.0230001(2147-183CIP)	1728

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EXAMINER	
DIBRINO, MARIANNE NMN	

ART UNIT	PAPER NUMBER
1644	

MAIL DATE	DELIVERY MODE
10/15/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/684,268	MONTERO-JULIAN ET AL.	
	Examiner	Art Unit	
	DiBrino Marianne	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 June 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *68-85* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *68-85* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *7/1/08,8/21/08,4/30/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. ***The Art Unit location and the Examiner of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1644.***

2. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 6/26/08 has been entered.

Applicant's amendment filed 6/26/08 is acknowledged and has been entered.

Newly added claims 68-76, 78 and 80-85 read upon the elected Group and species.

Upon consideration of the prior art, the species in newly added claim 77 and the species of HLA-B*0702 recited in newly added claim 79 are also being included in examination.

Claims 68-85 are presently being examined.

3. Reference "NPL67" in Applicant's Form 1449 filed 8/21/08 and references "NPL43" and "NPL35" in Applicant's Form 1449 filed 7/1/08 have been crossed out because they are not complete citations. Reference "AF" in Applicant's form 1449 filed 4/30/07 has been crossed out because it can not be found in the file or Applicant has not provided it. It will be considered in the next Office Action. It would expedite prosecution if Applicant would send in a copy of the reference.

4. The objection to the specification, the claim objections and the rejection of claims 5 and 8 under 35 USC 112, second paragraph, of record in the prior Office Action have been withdrawn in light of Applicant's amendment to the claims filed 6/28/08. In addition, the following applies:

(a) The 102(b) rejection of record in the prior Office Action has been withdrawn due to Applicant's said claim amendments and because Applicant is correct in stating that Altman *et al* do not teach a chimeric [human/murine] MHC class I.

(b) The 103(a) rejections of record in the prior Office Action of claims 6 and 7 over Altman in view of Becker and of claims 13 and 17-18 over Altman *et al* in view of Jager *et al* and of claims 23 and 24 over Altman *et al* in view of Zuk *et al* (and of claims 25 and 26 further in view of Schutzer) have been withdrawn in

view of Applicant's said claim amendments and because Altman *et al* do not teach a chimeric human/murine MHC class I.

(c) the 103(a) rejections of record in the prior Office Action of claims 13, 17 and 18 over Altman *et al* in view of Hildebrand and of claim 19 over Altman *et al* in view of Jager or alternatively in view of Hildebrand *et al* and further in view of Marin *et al* have been withdrawn in view of Applicant's said claim amendments, because Altman *et al* do not teach a chimeric human/murine MHC class I, and because the limitations recited in newly added instant claims 81 and 82 appear to be intended uses in the instant product claims.

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:
> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 70-73 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

The amendatory material not supported by the originally filed disclosure is as follows:

a. "wherein said solid surface is coated with a first binding ligand, which is connected to said monomer" recited in instant claim 70. The disclosure at [0086] is that the second ligand is connected to or within the MHC monomer, and the monomer may be immobilized to a surface either directly or indirectly, *e.g.*, via an anchoring or connecting entity. That is, only an indirect connection of the monomer to the first binding ligand is supported by the originally filed disclosure.

b. "a second binding ligand, which is attached to said monomer" recited in instant claim 71. The originally filed disclosure is to attachment of the C-terminal end of the monomer to the second binding ligand.

Applicant points to support for claims 70-73 at paragraphs [0077], [113]-[116] of the instant specification and in original claims 8-10.

However, the disclosure does not provide support as enunciated supra.

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:
> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 81 and 82 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention.

a. Claim 81 is indefinite in the recitation of "wherein said monomer incorporates a MHC-binding peptide in a solution" because it is not clear what is meant (see below).

b. Claim 82 is indefinite in the recitation of "wherein said monomer is recognized by a monoclonal antibody..." because it is not clear what is meant (see below).

It is unclear whether the recited limitations refer to intended uses in the claimed product or if they refer to inherent properties of the claimed product.

9. For the purpose of prior art rejections, the filing date of the instant claims 70-73 is deemed to be the filing date of the instant application, *i.e.*, 10/10/03, as the parent application does not support the claimed limitations of the instant application as enunciated at item #6 supra. The locations in the specification of the said parent application pointed to by Applicant for support, do not provide said support.

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

11. Claims 68-78 and 80-85 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 01/90747 A2 (IDS reference in Form 1449 filed 7/1/08) in view of Alexander *et al* (J. Immunol. 1997, 159: 4753-4761).

WO 01/90747 A2 teaches MHC class I monomers comprising the $\alpha 1 \alpha 2$ and $\alpha 3$ domains, $\beta 2m$, and optionally an antigenic peptide, bound to a solid surface such as a bead or microtiter plate, said binding being through attachment of avidin or streptavidin to the solid surface and the subsequent interaction with biotinylated MHC class I (the biotin attached to the C-terminal end of the monomer). WO 01/90747 A2 further teaches using the immobilized monomers to study T cell binding to MHC class I and for detecting agents that can modulate said binding. WO 01/90747 A2 teaches kits comprising the MHC molecules, such as HLA-A2 and HLA-B7(see entire reference, for example, abstract, lines 23-29 on page 7, lines 5-26 on page 13, lines 20-31 on page 14, lines 4-21 on page 51, lines 9-10 on page 53, lines 4-5 on page 54, and claims, especially claims 1, 124, 127, 130-132).

WO 01/90747 A2 does not teach wherein the MHC class I comprises a human MHC class I domain and a murine MHC class I domain, nor that the MHC molecule bound to the solid support is comprised in a kit.

Alexander *et al* teach a chimeric MHC class I molecule comprising human HLA-A11 $\alpha 1\alpha 2$ domains with a murine H-2K^b $\alpha 3$ domain. Alexander *et al* teach that these constructs were expressed in mice, thus making transgenic mice, and that it is necessary to use the murine $\alpha 3$ domain in order to preserve the species-specific interactions between CD8 [positive T cells in the transgenic mice that interact with class I] and the $\alpha 3$ domain of the class I molecule.

It would have been prima facie obvious to modify the solid support taught by WO 01/90747 A2 by substituting the transgenic class I construct taught by Alexander *et al* for the human class I construct taught by WO 01/90747 A2 .

One of ordinary skill in the art at the time the invention was made would have been motivated to do this in order to study transgenic T cells and agents that interfere with binding of those T cells to the transgenic HLA-A11/H-2K^b class I molecule.

With regard to the limitation recited in instant claim 81, it is an expected property of the art molecule that it is able to incorporate an MHC-binding peptide in the instance of empty MHC complexes, *i.e.,* the HLA complexes lacking a binding peptide in the peptide binding groove can acquire a peptide. It is also an expected property of occupied MHC molecules (those with a bound peptide) that given the binding of MHC to peptide is a noncovalent, reversible interaction even with cell surface bound MHC/peptide complexes, absent evidence to the contrary, that the MHC molecules would be capable of releasing peptide and renaturing to re-incorporate peptide.

With regard to the limitation recited in instant claim 82, it is an expected property of the art MHC molecule, particularly since it is bound to peptide and can be recognized by T cells specific for the appropriate MHC/peptide complex, that the MHC class I molecule is in the proper conformation to be bound by a monoclonal antibody that distinguishes between a class I molecule bound to an MHC binding peptide versus one that lacks such a peptide.

It would have been prima facie obvious to have included the MHC molecule bound to the solid support taught by the combination of WO 01/90747 A2 and Alexander *et al* in a kit.

One of ordinary skill in the art at the time the invention was made would have been motivated to do this because WO 01/90747 A2 teaches placing the MHC class I molecule in a kit and for convenience.

It would have been prima facie obvious to have provided the MHC bound to a solid support in a dried form.

One of ordinary skill in the art at the time the invention was made would have been motivated to do this for convenience of handling and storage.

12. Claims 68-77 and 80-84 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 5,635,363 (of record) in view of Alexander *et al* (J. Immunol. 1997, 159: 4753-4761).

US 5,635,363 discloses a system comprising a solid surface such as beads or a microtiter plate) to which is attached one or more MHC monomers, and its use for detecting and/or separating antigen-specific T cells. US 5,635,363 discloses using the $\alpha 1\alpha 2$ and $\alpha 3$ domains of MHC heavy chain of class I molecules such as HLA-A, -B or –C, as well as the $\beta 2m$ light chain. The two subunits may be combined with an antigenic peptide(s) or the peptide(s) may be added later. US 5,635,363 discloses that the MHC molecule may be biotinylated at the C-terminus and then bound to streptavidin or avidin, the latter two of which may be bound to an insoluble solid support such as beads or microtiter plates. US 5,635,363 discloses that the T cells may be from any source, usually having the same species of origin as the MHC heterodimer (see entire reference, for example, abstract, column 1 at lines 55-67, paragraph spanning columns 4-5, column 6 at lines 51-65, column 7 at lines 12-15, column 8 at lines 4-8).

US 5,635,363 does not teach wherein the MHC class I comprises a human MHC class I domain and a murine MHC class I domain.

Alexander *et al* teach a chimeric MHC class I molecule comprising human HLA-A11 $\alpha 1\alpha 2$ domains with a murine H-2K^b $\alpha 3$ domain. Alexander *et al* teach that these constructs were expressed in mice, thus making transgenic mice, and that it is necessary to use the murine $\alpha 3$ domain in order to preserve the species-specific interactions between CD8 [positive T cells in the transgenic mice that interact with class I] and the $\alpha 3$ domain of the class I molecule.

It would have been prima facie obvious to modify the solid support taught by US 5,635,363 by substituting the transgenic class I construct taught by Alexander *et al* for the human class I construct taught by WO 01/90747 A2 .

One of ordinary skill in the art at the time the invention was made would have been motivated to do this in order to study transgenic T cells and agents that interfere with binding of those T cells to the transgenic HLA-A11/H-2K^b class I molecule.

With regard to the limitation recited in instant claim 81, it is an expected property of the art molecule that it is able to incorporate an MHC-binding peptide in the instance of empty MHC complexes, *i.e.*, MHC complexes lacking a binding peptide in the peptide binding groove. It is also an expected property of (peptide) occupied MHC molecules that given the binding of MHC to peptide is a noncovalent, reversible interaction, absent evidence to the contrary, that the MHC molecules would be capable of releasing peptide and renaturing to re-incorporate peptide.

With regard to the limitation recited in instant claim 82, it is an expected property of the art MHC molecule, particularly since it is bound to peptide and can be recognized by T cells specific for the appropriate MHC/peptide complex, that the MHC class I molecule is in the proper conformation to be bound by a monoclonal antibody that distinguishes between a class I molecule bound to an MHC binding peptide versus one that lacks such a peptide.

It would have been prima facie obvious to have provided the MHC bound to a solid support in a dried form.

One of ordinary skill in the art at the time the invention was made would have been motivated to do this for convenience of handling and storage.

13. Claims 78, 79 and 85 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 5,635,363 (of record) in view of Alexander *et al* (J. Immunol. 1997, 159: 4753-4761) as applied to claims 68-77 and 80-84 above, and further in view of US 4,208,479 (of record).

US 5,635,363 and Alexander *et al* have been discussed supra. Alexander *et al* also teach a chimeric MHC class I molecule comprising human HLA-A2.1 (*i.e.,* HLA-A*0201) $\alpha 1 \alpha 2$ domains with a murine H-2K^b $\alpha 3$ domain. Alexander *et al* teach HLA-B class I molecules (especially introduction section).

The combination of US 5,635,363 and Alexander *et al* does not teach that the solid support comprising the MHC class I molecule is in a kit.

US 4,208,479 discloses that reagents for performing assays may be provided in dry form, the advantages of which are their stability, shelf life and convenience over wet forms. US 4,208,479 further discloses that in performing assays, it is a matter of substantial convenience to provide the needed reagents in a kit (especially column 2 at lines 49-54, column 22 at lines 36-39 and column 22 at lines 20-68).

It would have been prima facie obvious to have included the MHC molecule bound to the solid support taught by the combination of US 5,635,363 and Alexander *et al* in a kit, including chimeric MHC class I molecules of the classes taught by Alexander *et al*.

One of ordinary skill in the art at the time the invention was made would have been motivated to do this because US 5,635,363 teaches placing the MHC class I molecule in a kit and for convenience.

It would also have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have provided the system taught by the combined references in dried form.

One of ordinary skill in the art at the time the invention was made would have been motivated to do this because US 4,208,479 discloses the advantages of providing reagents in dried form.

Claim 79 is included in this rejection because HLA-B*0702 is a subtype of the HLA-B7 class I molecule taught by Alexander *et al*.

14. Claim 72 is objected to because of the following informality: Claim 72 contains a spelling error, *i.e.*, "an" avidin or streptavidin. Appropriate correction is required.

15. No claim is allowed.

16. Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Marianne DiBrino whose telephone number is 571-272-0842. The Examiner can normally be reached on Monday, Tuesday, Thursday and Friday.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Eileen B. O'Hara, can be reached on 571-272-0878. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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September 22, 2008

/G.R. Ewoldt/
Primary Examiner, Art Unit 1644